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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/845,042	04/27/2001	Filippo Belardelli	B-4161 618742-8	1462

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YOUNG & THOMPSON
745 SOUTH 23RD STREET
2ND FLOOR
ARLINGTON, VA 22202

EXAMINER	
EWOLDT, GERALD R	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 10/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/845,042	BELARDELLI ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *5/20/05 and 8/01/05*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *54-58,61-63 and 65-71* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *54-58,61-63 and 65-71* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed 8/01/05 in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's amendment and remarks, filed 5/20/05, have been entered.

2. Claims 54-58, 61-63, and 65-71 are pending and under examination.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 54-58, 61-63, and 65-70 stand rejected under 35 U.S.C. 112, first paragraph, as based on a disclosure which is not enabling. Elements critical or essential to the practice of the invention, but not included in the claims are not enabled by the disclosure, for the reasons of record.

As set forth previously, the specification discloses that *only* cultures employing 1000 IU/ml IFN resulted in functional DCs. Accordingly, the use of 1000 IU/ml IFN in the claimed method would be considered essential to the instant invention. Likewise, *all* disclosed cultures employed 500 IU/ml GM-CSF. Thus, the use of 500 IU/ml GM-CSF in the claimed method would also be considered essential to the instant invention.

Applicant's arguments, filed 5/20/05, have been fully considered but they are not persuasive. Applicant argues that Figure 3 shows different effective doses of type I IFN. Applicant argues that GM-CSF is not essential but that the claims have been amended to recite its use in the interest of advancing prosecution. Applicant argues that as a matter of law the Examiner has the initial burden of establishing a basis for questioning enablement.

It remains the Examiner's position that the instant disclosure does not adequately enable the broadly claimed method. Regarding the Examiner's initial burden of establishing a basis for questioning enablement, Applicant is advised that MPEP 2164.03 clearly states that physiological processes are generally considered to be unpredictable. Given this inherent unpredictability, an enabling disclosure commensurate in scope with the breadth of the claims is required. Applicant's own disclosure provides additional basis in the teaching that 100 U of IFN was ineffective in the claimed method. Clearly then, not all concentrations of IFN are effective, thus, it is just as likely that not all concentrations of GM-CSF would prove effective either. Indeed, it is likely that some synergism between the effects of IFN and GM-CSF is responsible for the surprisingly quick partial maturation of the monocytes into DCs of the claimed method. Also note that the Inventor's own work, Santini et al. (2000, IDS), characterizes the instant findings as reporting "that type I IFNs induce a rapid differentiation of freshly isolated GM-CSF-treated human monocytes into short-lived DCs…", and in that work the Inventor's again used 500 IU/ml GM-CSF and 500 or 1000 IU/ml IFN in all effective instances. Accordingly, Applicant cannot now simply assert that any concentration of GM-CSF, e.g., 1 IU/ml, and concentrations of IFN below 500 IU/ml, would be effective in the claimed method.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 55 and 62 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

As set forth previously, Specifically:

A) Claim 55 is vague and indefinite as they recite a method employing "any synthetic type I IFN" as the term is not defined in the specification.

B) Claim 62 is vague and indefinite as they recite a method employing a "maturation agent" as the term is not defined in the specification.

Applicant's arguments, filed 5/20/05, have been fully considered but they are not persuasive.

Regarding A), Applicant argues that synthetic type I IFN include synthetic consensus IFN, citing pages 6 and 17 of the

specification, and also submits De Maeyer et al. (1983) citing page 102.

Applicant is advised that pages 6 and 17 of the specification do not include a definition for "any synthetic type I IFN", nor do they disclose "synthetic consensus IFN", and regardless, a single species would not define the claimed genus. Applicant is further advised that the teachings of De Maeyer et al. (page 102 is presumably actually page 120), "Synthetic genes coding for IFNαs were designed to optimize codon use for *E. coli* but also to allow construction of sub-gene duplexes with unique restriction sites at either end," also does not further define the claimed genus of "any synthetic type I IFN".

Regarding B), Applicant argues that the skilled artisan would know what kind of agent to employ and cites page 4 of the specification.

As set forth previously, an attorney's assertion regarding the knowledge of the skilled artisan is not convincing. Regarding the disclosure at page 4 of the specification, that "DC maturation can be driven by the addition of TNF-alpha, IL-1, LPS, monocyte-conditioned medium or sCD40L", the cite does not define the term "maturation agent", i.e., there is no teaching that the maturation agent of the claims is a substance that "drives DC maturation".

7. Claims 54-58, 61-63, and 65-71 stand rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

As set forth previously, The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A) A process ... with a Type I IFN concentration greater that 400 IU/ml (Claims 54 and 63).

B) A process ... in the absence of IL-4 (Claims 54, 63, 68) or wherein IL-4 is absent (Claim 69).

Applicant's arguments, filed 5/20/05, have been fully considered but they are not persuasive.

Regarding A), Applicant argues that the disclosure of greater than 100 IU/ml and 400-1000 IU/ml support the concept of greater than 400 IU/ml.

It remains the Examiner's position that the new genus of IFN concentrations of greater than 400 IU/ml includes concentrations not disclosed in the specification, e.g., 1100 IU/ml.

Regarding B), Applicant argues that the disclosures at pages 19 and 20 of the specification support the claimed limitation

It remains the Examiner's position that the disclosures at pages 19 and 20 of the specification do not disclose the claimed limitation in the claimed context, i.e., in a generic method of deriving DCs from PBMC or monocytes. The disclosure comprises the results of specific experiments and not the generic method of the claims.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 54-58, 61-63, and 65-71 stand rejected under 35 U.S.C. 102(b) as being clearly anticipated by Paquette et al. (1998), for the reasons of record set forth in the action mailed 1/28/04.

Applicant's arguments, filed 5/20/05, have been fully considered but they are not persuasive. Applicant argues that the reference does not contemplate the culturing of DCs in as little as 3 days. Further, the cells of the reference are no the cells of the instant claims.

It remains the Examiner's position that the method of the reference is the method of the instant claims. In particular, note the recitation of "a process … comprising … isolating said DCs after 3 days in culture". "Comprising" indicates open language, "after 3 days in culture" means 3 *or more* days in culture, thus, the 7 day culture of the reference is

encompassed by the culture of the instant claims. Regarding differences in results, said differences represent merely the realities of biological processes. i.e., results vary. As the same method steps were performed in the reference as are recited in the instant claims, the reference anticipates the method of the instant claims. Additionally, if the method of the reference were to be considered to be limited to a method that comprised only the disclosed results, then the method of the instant claims would necessarily be likewise limited to a method comprising only the instantly disclosed results, e.g., a method that resulted in 36% CD14 expression.

10. The following are new grounds for rejection.

11. Claim 61 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the claim depends from canceled Claim 60.

12. Claims 54-58, 62, and 68-71 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically, the recitation of "isolating said cells after culturing said cells for 3 days" (Claim 54), or "isolating said dendritic cells after 3 days of culture" (Claim 68), or "isolating said cells after 3 days of culture" (Claim 69).

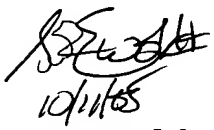
Applicant does not cite any support for the new limitation and none has been found.

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's

voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

15. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see www.uspto.gov/ebc/newusers.html. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



10/11/05

G.R. Ewoldt, Ph.D.
Primary Examiner
Technology Center 1600